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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/893,344	06/28/2001	Michal Eisenbach-Schwartz	EIS-SCHWARTZ=21	1157

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BROWDY AND NEIMARK, P.L.L.C.
624 Ninth Street, N.W.
Washington, DC 20001

EXAMINER
NICHOLS, CHRISTOPHER J

ART UNIT	PAPER NUMBER
1647	12

DATE MAILED: 09/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/893,344	EISENBACH-SCHWARTZ ET AL.	
	Examiner	Art Unit	
	Christopher Nichols, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 July 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 32-63 is/are pending in the application.

4a) Of the above claim(s) *36 39 41 44 -47 49 51 52 55 57 61-63* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-35,37,38,40,42,43,48,50,53,54,56 and 58-60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 32-63 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of Application, Amendments, and/or Claims

1. The Amendment filed 7 July 2003 (Paper No. 9) has been received and entered in full. Claims 1-31 have been cancelled and claims 32-63 have been added.

2. Newly submitted claims 36, 39, 41, 44, 45, 46, 47, 49, 51, 52, 55, 57, 61, 52, and 63 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the Restriction Election Requirement (Paper No. 4, 25 September 2002) delineated two Groups: Group I drawn to administration of poly-Glu,Tyr and Group II drawn to administration of poly-Glu,Tyr activated T-cells. Applicant elected with traverse Group I and "glaucoma" as the species.

3. Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 36, 39, 41, 44, 45, 46, 47, 49, 51, 52, 55, 57, 61, 52, and 63 withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

4. Concerning the Applicant's continued traverse of the Restriction Requirement as set forth in Office Action Paper No. 4 (25 September 2002). It was made Final in the previous Office Action (Paper No. 7 January 2003) and is still in effect as noted above. Further, it is further noted that upon reaching allowable subject matter, rejoinder will be considered.

5. Applicant's summary of the Interview (Paper No. 8, 26 May 2003) is acknowledged.

Withdrawn Objections And/Or Rejections

6. The objection to the Specification as set forth at pp. 3 ¶6 in the previous Office Action (Paper No. 6, 7 January 2003) is hereby *withdrawn* in view of Applicant's amendments (Paper No. 9, 7 July 2003).

7. The objection to the Drawings as set forth at pp. 3 ¶7 in the previous Office Action (Paper No. 6, 7 January 2003) is hereby *withdrawn* in view of Applicant's amendments (Paper No. 9, 7 July 2003).

8. The objection to the claims as set forth at pp. 3-4 ¶8-10 in the previous Office Action (Paper No. 6, 7 January 2003) is hereby *withdrawn* in view of Applicant's cancellation of said claims (Paper No. 9, 7 July 2003).

9. The rejection of claims 1-9 and 14-15 under 35 U.S.C. 112 ¶1 as set forth at pp. 4-8 ¶11-18 in the previous Office Action (Paper No. 6, 7 January 2003) is *moot* in view of Applicant's cancellation of said claims (Paper No. 9, 7 July 2003).

10. All objections and rejections not herein reiterated, maintained, or set forth are hereby *withdrawn*.

New Objections And/Or Rejections

Claim Objections

11. Claims **32, 33, 34, 35, 37, 38, 40, 42, 43, 48, 50, 53, 54, 56, 58, 59, and 60** are objected to because of the following informalities: said claims recite non-elected subject matter. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims **32, 33, 34, 35, 37, 38, 40, 42, 43, 48, 50, 53, 54, 56, 58, 59, and 60** are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a *method of lessening retinal ganglion cell (RGC) death and/or lessening damage to the optic nerve arising from a group consisting of glaucoma, increased intraocular pressure, and glutamate toxicity comprising administration of an effective amount of poly-Glu,Tyr,* does not reasonably provide enablement for *a method for reducing secondary neuronal degeneration, or for reducing secondary neuronal degeneration that follows the primary neuronal damage of an injury, ameliorating the effects of an injury or disease that causes neuronal degeneration of the central or peripheral nervous system.* The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims for the reasons set forth in the previous Office Action (Paper No. 6, 7 January 2003).

13. The Applicant traverses the rejection under 35 U.S.C. §112 ¶1 for the following reasons: **(a)** the presentation by the Inventor (Prof. Eisenbach-Schwartz) on 26 May 2003 demonstrated a reduction to practice of COP-1 and "NS-antigens" for use in the reduction of neuronal

degeneration caused by the degenerative effects of any disease or for reducing secondary neuronal degeneration that follows the primary neuronal damage of any injury and **(b)** 38 references are listed on pp. 19-22 and select references are discussed on pp. 22-23 of the Applicant's Response (Paper No. 9, 7 July 2003). Applicant's argument has been taken into consideration and is not found persuasive for the following reasons.

14. On **"(a)"**, the Examiner attended the aforementioned interview and the Inventor (Prof. Eisenbach-Schwartz) did show data concerning the use of COP-1 and "NS-antigens" as therapeutics to reduce secondary neuronal degeneration. However, currently, no Declaration under 37 C.F.R. §1.132 has been submitted in the instant application to make of record evidence that poly-Glu,Tyr (pEY) administration has the full range of effects as claimed. The specification fails to provide any guidance for the successful treatment of any other form of injury, disorder, or disease in addition to glaucoma, increased intraocular pressure, and glutamate toxicity of RGC or the optic nerve using the claimed method, and since resolution of the various complications in regards to the efficacy of a therapy in such a massive genus is highly unpredictable, one of skill in the art would have been unable to practice the invention without engaging in undue trial and error experimentation. In order to practice the invention using the specification and the state of the art as outlined below, the quantity of experimentation required to practice the invention as claimed *in vivo* would require the *de novo* determination of signs and symptoms of each disease, disorder, and injury to correlate relief with the pEY administration. In the absence of any guidance from the specification, the amount of experimentation would be undue, and one would have been unable to practice the invention over the scope claimed.

15. Additionally, a person skilled in the art would recognize that predicting the efficacy of using a specific therapy based solely on its performance in a single model is highly problematic since the Applicant has not provided any secondary evidence to support the claims which cover the large geneses disease and injury (see MPEP 2164.02). The only evidence on record is for glaucoma or more broadly, retinal ganglion cell death due to intraoculator pressure or glutamate toxicity, and is not predicative of any of the other listed neuronal diseases, disorders, or injuries. Thus, although the specification prophetically considers and discloses general methodologies of using the claimed method as a therapy for a large and diverse genus, such a disclosure would not be considered enabling since the state of central nervous system disease, injury, and disorder is highly unpredictable.

16. Concerning "**(b)**", any references which the Applicant wishes for the Examiner to review and make of record should be supplied in the form of an Information Disclosure Statement pursuant to 37 C.F.R. §1.98(a)(1) which requires a list of all patents, publications, or other information submitted for consideration by the Office. It has been placed in the application file, but the information referred to therein has not been considered. Submission of the proper PTO-1449 form with copies of the references listed therein will be taken into due consideration by the Examiner.

17. On the instant application, the claims are drawn very broadly to methods of using administration of poly-Glu,Tyr (pEY) to treat a large range of injuries, maladies, deficiencies, diseases, and disorders in humans.

18. The specification teaches that activated T-cells that recognize an antigen of the nervous system of the patient can be used as therapeutics. For instance, T-cells specific for myelin basic

protein (MBP) has been shown to be effective in providing relief in rat models of partially crushed optic nerve. The specification teaches that administration of pEY will lessen the degree of RGC death due to intraocular pressure in a mouse model of glaucoma.

19. The factors listed below have been considered in the analysis of enablement:

(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

20. The following references are cited herein to illustrate the state of the art of glaucoma.

21. The art teaches that administration of COP-1 (synthetic co-polymer) increased retinal ganglion cell (RGC) survival in a glutamate induced mouse model of glaucoma [Schori *et al.* (13 March 2001) "Vaccination for protection of retinal ganglion cells against death from glutamate cytotoxicity and ocular hypertension: Implications for glaucoma." PNAS **98**(6): 3398-3403]. In addition, the art teaches that retinal ganglion cell (RGC) death is a hallmark of several ophthalmic diseases including glaucoma, retinal ischemia, anterior ischemic optic neuropathy and optic nerve trauma [Sucher *et al.* (1997) "Molecular Basis of Glutamate Toxicity in Retinal Ganglion Cells." Vision Res. **37**(24): 3483-3493). The art also teaches that administration of MBP has salubrious effects in lessening the damage resulting from spinal cord injury [Hauben *et al.* (1 September 2000) "Passive or Active Immunization with Myelin Basic Protein Promotes Recovery from Spinal Cord Contusion." The Journal of Neuroscience **20**(17): 6421-6430, Hauben *et al.* (August 2001) "Posttraumatic therapeutic vaccination with modified myelin self-

antigen prevents complete paralysis while avoiding autoimmune disease." The Journal of Clinical Investigation **108**(4): 591-599].

22. As discussed above, none of these references show evidence to support the full scope of the claims for the method of using poly-Glu,Tyr as a therapeutic. In essence, the claims as written are an invitation to experiment with poly-Glu,Tyr due to the absence of any guidance for practicing the method as claimed. First the skilled artisan is invited to administer poly-Glu,Tyr to a wide range of clinical situations and then assess the success of each individual situation. Thus the skilled artisan is confronted with an undue burden of experimentation in the absence of guidance from the instant Specification or the prior art to practice the full-breadth of the claims.

23. Claim **43** is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

24. The term "critical" in claim 43 is a relative term which renders the claim indefinite. The term "critical" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The metes and bounds of said term are not clearly defined in the Specification or the prior art.

Summary

25. Claims **32, 33, 34, 35, 37, 38, 40, 42, 43, 48, 50, 53, 54, 56, 58, 59, and 60** are hereby rejected.

26. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Christopher James Nichols, Ph.D.** whose telephone number is 703-305-3955. The examiner can normally be reached on Monday through Friday, 8:00AM to 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Gary Kunz, Ph.D.** can be reached on 703-308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications. The fax phone numbers for the customer service center is 703-872-9305

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Elizabeth C. Kemmerer

CJN
August 26, 2003

ELIZABETH KEMMERER
PRIMARY EXAMINER